BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Paper No. 27

Application Number: 09/096,070
Filing Date: June 11, 1998
Appellant(s): HILLMAN ET AL.

Richard C. Eckstrom
Michelle M. Stempien
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 2/7/2002.

(1) Real Party in Interest
A statement identifying the real party in interest is contained in the brief.
(2) Related Appeals and Interferences
A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.
(3) Status of Claims
The statement of the status of the claims contained in the brief is correct.
(4) Status of Amendments After Final
The appellant's statement of the status of amendments after final rejection contained in the brief is correct.
(5) Summary of Invention
The summary of invention contained in the brief is correct.
(6) Issues
The appellant's statement of the issues in the brief is correct.
(7) Grouping of Claims
Appellant's brief includes a statement that claims 1, 32, 33 and 36 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).
(8) Claims Appealed
The copy of the appealed claims contained in the Appendix to the brief is correct.
(9) Prior Art of Record
Rockett, et. al., Differential gene expression in drug metabolism and toxicology: practicalities, problems and potential, 29 Xenobiotica No. 7, 655, 656 (1999). (Newly cited in Brief.).

Nuwaysir, et. al., Microarrays and Toxicology: The Advent of Toxicogenomics, 24 Molecular Genesis 153 (1999). (Newly cited in Brief.).

Sandra Steiner and N. Leigh Anderson, Expression profiling in toxicology -- potentials and limitations, 112-13 Toxicology Letters 467 (2000). (Newly cited in Brief.).

Brenner, Assessing sequence comparison methods with reliable structurally identified distant evolutionary

relationships, Vol. 95, pages 6073-6078 (1998). (Newly cited in Brief).

(10) Grounds of Rejection
The following ground(s) of rejection are applicable to the appealed claims:
Issues 1 and 2
Claims 1, 28 and 32-36 stand rejected under 35 U.S.C. § 101 and 35 USC (112, first paragraph for reasons of record set forth in Paper No. 20, 10/30/2000 and Paper No. 22, 4/17/2001.
As stated therein, It is clear from the instant specification that the HPURR polypeptide has been isolated because of its similarity to known proteins. However, it is commonly known in the art that sequence-to-function methods of assigning protein function are prone to errors (Doerks et al.1998). These errors can be due to sequence similarity of the query region to a region of the alleged similar protein that is not the active site, as well as homologs that did not have the same catalytic activity because active site residues of the characterized family were not conserved Doerks et al. page 248, column 3, fourth and fifth paragraphs). Inaccurate use of sequence-to-function methods have led to significant function-annotation errors in the sequence databases (Doerks et al. page 250, column 1, third paragraph). There is little doubt that, after complete characterization, this protein will probably be found to have a patentable utility. This further characterization, however, is part of the act of invention and until it has been undertaken Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in Brenner v. Manson, 148 USPQ 689 (Supreme Court, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anticancer activity was alleged to be potentially useful as an antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 USC § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to a polypeptide which has an as yet undetermined function or biological significance. Until some actual and specific significance can be attributed to the protein identified in the specification as HPURR the instant invention is incomplete. The polypeptide of the instant invention is known to be structurally analogous to proteins which are known in the art as purinergic receptors. In the absence of knowledge of the natural substrate or biological significance of this protein, there is no immediately obvious patentable use for it. To employ a protein of the instant invention in the identification of substances which inhibit its activity is clearly to use it as the object of further research which has been determined by the courts to be a non-patentable utility. Since the instant specification does not disclose a "real world" use for HPURR then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 USC § 101 as being useful.

Claims 1, 28 and 32-36 also stand rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.
Issue 3
Claims 32 and 36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 1, does not reasonably provide enablement for a naturally occurring amino acid sequence with 90% amino acid sequence identity to SEQ ID NO: 1, for reasons of record set forth in Paper No. 22, 4/17/2001. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.
Claims 32 and 36 are overly broad in the recitation of "at least 90% identical" since no guidance is

provided as to which of the myriad of polypeptide species encompassed by the claim will retain the characteristics of a purinoceptor. The specification (page 6, line 29 to page 7, line 5) discloses that variants of the polypeptide can be generated by conservative or nonconservative changes, deletions and insertions but does not disclose any actual or prophetic examples on expected performance parameters of any of the possible muteins of HPURR. However, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation-inhibiting factor (GIF) protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

There is no guidance provided in the specification as to how one of ordinary skill in the art would generate an HPURR polypeptide other than those exemplified in the specification. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. Given the breadth of claims 32 and 36 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Issue 4

Claims 1, 32-33 and 36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record set forth in Paper No. 22, 4/17/2001.

These claims are drawn to biologically active fragments and polypeptides that are at least 90% identical to SEQ ID NO: 1 and are genus claims. According to the specification (page 6, line 29 to page 7, line 7), the term variant means a protein having one or more amino acid substitutions, deletions, insertions and/or additions made to SEQ ID NO: 1. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to SEQ ID NO: 1. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Although the specification states that these types of changes are routinely done in the art, the specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO: 1 alone is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

(11) Response to Argument

Issues 1 and 2

Appellants summarize case law on the utility requirement at pages 7-8 of the Brief. The essential disagreement appears to be the interpretation of what constitutes a specific, substantial and credible utility, as will be explained more fully below.

The similarity of the claimed polypeptide to another polypeptide of known, undisputed utility by itself demonstrates utility beyond the reasonable probability required by law. Brief at 5. The Examiner must accept the applicant's demonstration that the claimed polypeptide is a member of the P2x receptor firmly and that utility is proven by a reasonable probability unless the Examiner can demonstrate through evidence or sound scientific reasoning that a person of ordinary skill in the art would doubt utility. Brief at 9-10 bridging paragraph.

Appellant argues that homology has been established between the HPURR protein with 51% identity to a human purinergic receptor. However, as set forth in Paper No. 20, 10/30/2000 it is clear that, although there is a 51% identity between the human purinergic receptor and SEQ ID NO: 1, there is a 49% dissimilarity between SEQ ID NO: 1 and the sequence of human purinergic receptor, and the effects of these dissimilarities upon protein structure and function cannot be predicted. It is commonly known in the art that sequence-to-function methods of assigning protein function are prone to errors (Doerks et al.1998). These errors can be due to sequence similarity of the query region to a region of the alleged similar protein that is not the active site, as well as homologs that did not have the same catalytic activity because active site residues of the characterized family were not conserved (Doerks et al. page 248, column 3, fourth and fifth paragraphs). Inaccurate use of sequence-to-function methods have led to significant function-annotation errors in the sequence databases (Doerks et al. page 250, column 1, third paragraph). The art further teaches that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. It is further known that while many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions. Proteins can be sensitive to alterations of even a single amino acid in a sequence. It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. For instance, one amino acid substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages. This demonstrates that even a single amino acid substitution will often dramatically affect the biological activity and characteristics of a protein.

Clearly, with 49% dissimilarity to the human purinergic receptor, the function of the SEQ ID NO: 1 polypeptide could not be predicted, based on sequence similarity with the human purinergic receptor, nor would it be expected to be the same as that of the human purinergic receptor. The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed polypeptide. Because the claimed invention is not supported by a well-established, substantial and specific asserted utility for the reasons set forth, credibility of any utility cannot be assessed.

Based upon the art recognized errors inherent in sequence-function methods of assigning protein function, and the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex, and the fact that the change of a single amino acid can radically alter protein function, and absent sufficient evidence to the contrary, a preponderance of the evidence demonstrates that the nucleic acid encoding a polypeptide with an amino acid sequence as set forth in SEQ ID NO: 1 lacks a well-established, specific and substantial utility.

Appellant argues that the Voet et al. document, relating to the hemoglobin/sickle-cell anemia gene

sequences, is the exception, not the rule. In fact, Appellants assert that this is a case of the exception proving the rule. Brief at 18. However, the Voet reference demonstrates the large effect that even a single amino acid change can have on protein structure and function. This is not an exception to the rule but a demonstration of the unpredictability of the protein art when trying to predict the function of a protein given only the primary amino acid sequence.

Appellant further cites Brenner to argue that sequence homology in excess of 40% over 70 or more amino acid residues yields a high probability of functional homology. However, while this may be an indication of the family to which the protein belongs, as the Voet reference demonstrates, even small differences in protein structure can have large effects on protein function.

Even if, arguendo, the HPURR protein is found to be a G-protein coupled receptor, it is an orphan receptor. Since the ligand to this receptor is unknown, the function of the protein is also unknown. Neither the specification nor the art of record disclose any diseases or conditions associated with the function or expression of the HPURR protein, therefore, there is no "real world" context of use. Further research to identify or reasonably confirm a "real world" context of use is required.

Appellant argues that as demonstrated by the Furness Declaration (Dec. at ¶3), the person of ordinary skill in the art can achieve beneficial results from the claimed polypeptide is the absence of any knowledge as to the precise function of the protein. Brief at 7. The Furness Declaration argues that the claimed invention has specific, substantial, real-world utility by virtue of its use in toxicology testing, drug development and disease diagnosis through gene expression profiling. Brief at 10.

The question at issue is whether or not the broad general assertion that the claimed polypeptides might be used for some diagnostic application in the absence of a disclosure of which diagnostic application would be considered to be an assertion of a specific, substantial, and credible utility. The disclosure satisfies none of the three criteria See In re Kirk, 153 USPQ 48, 53 (CCPA 1967) (quoting the Board of Patent Appeals, "We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an Appellant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.")

First, Appellant argues, and cites the Furness Declaration (Dec. at ¶11, Brief at 11-12) as evidence, that toxicology testing is a well-established utility and concludes that the claimed polypeptides could be used in this manner and that the claimed invention possesses utility. Appellant further cites Rockett et al., Nuwaysir et al. and Steiner, as evidence that toxicology testing is now standard practice in the pharmaceutical industry. However, for a utility to be "well-established" it must be specific, substantial and credible. In this case all nucleic acids and genes are in some combination useful in toxicology testing. However, the particulars of toxicology testing with SEQ ID NO: 1 are not disclosed in the instant specification. Neither the toxic substances nor the susceptible organ systems are identified. Therefore, this is a utility which would apply to virtually every member of a general class of materials, such as any collection of proteins or DNA, but is only potential with respect to SEQ ID NO: 1. Because of this, such a utility is not specific and does not constitute a "well-established" utility. Further, because any potential diagnostic utility is not yet known and has not yet been disclosed, the utility is not substantial because it is not currently available in practical form. Moreover, use of the claimed polypeptide in an array for toxicology screening is only useful in the sense that the information that is gained from the array is dependent on the pattern derived from the array, and says nothing with regard to each individual member of the array. Again, this is a utility that would apply to virtually ever member of a general class of materials, such as any collection of proteins or DNA. Even if the expression of Appellant's individual polypeptide is affected by a test compound in an array for drug screening, the specification does not disclose any specific and substantial interpretation for the result, and none is known in the art. Given this consideration, the individually claimed polypeptide has no "well-established" use. The artisan is required to perform further experimentation on the claimed material itself in order to determine to what use any expression information regarding this polypeptide could be put.

With regard to drug discovery and development, (Dec. at ¶12) Appellant mentions expression profiling as one use of the claimed polypeptide in the instant application. Appellant states expression profiling is a method for identifying drug targets and characterize diseases. Such a profile is independent of the function of the genes or gene products. In the instant case, the claimed polypeptide can be used as one of many targets on a microarray to generate an expression profile. A transcript image thus generated

from lung tumor tissue can be compared, for example, with that from lung tumor tissue treated with a potential therapeutic compound in order to evaluate the efficacy of the compound.

However, there is no way to assess the meaning of any individual hit obtained from this procedure. The first requirement is that one must know the biological significance of the polypeptide which is being evaluated. Without this information, the results of the expression profile is useless because one would not know if the polypeptide expression should be increased or decreased or even what significance could be attributed to such changes in expression profiles.

Appellant further argues, citing the Furness Declaration (Brief at 8, Dec. at ¶9) the utility of the claimed polypeptide in the diagnosis of disease. However, in order for a polypeptide to be useful, as asserted, for diagnosis of a disease, there must be a well-established or disclosed correlation or relationship between the claimed polypeptide and a disease or disorder. The presence of a polypeptide in tissue that is derived from cancer cells is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the claimed polypeptide and the disease. If a molecule is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polypeptide to be used in a diagnostic manner. Many proteins are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the claimed polypeptide is either present only in cancer tissue to the exclusion of normal tissue or is expressed in higher levels in diseased tissue compared to normal tissue (i.e. overexpression). Evidence of a differential expression might serve as a basis for use of the claimed polypeptide as a diagnostic for a disease. However, in the absence of any disclosed relationship between the claimed polypeptide and any disease or disorder and the lack of any correlation between the claimed polypeptide with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. Congress intended that no patent be granted on a chemical compound whose sole utility consists of its potential role as an object of use-testing. Brenner, 148 USPQ at 696. The disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. § 101.

The Furness Declaration argues (Dec. at ¶10) that selectivity screening is a well-established utility and concludes that the claimed polypeptides could be used in this manner and that the claimed invention possesses utility. However, for a utility to be "well-established" it must be specific, substantial and credible. In this case all nucleic acids and genes are in some combination useful in selectivity screening. However, the particulars of selectivity screening with SEQ ID NO: 1 are not disclosed in the instant specification. Therefore, this is a utility which would apply to virtually every member of a general class of materials, such as any collection of proteins or DNA, but is only potential with respect to SEQ ID NO: 1. Because of this, such a utility is not specific and does not constitute a "well-established" utility. Further, because any potential diagnostic utility is not yet known and has not yet been disclosed, the utility is not substantial because it is not currently available in practical form. Moreover, use of the claimed polypeptide in an array for selectivity screening is only useful in the sense that the information that is gained from the array is dependent on the pattern derived from the array, and says nothing with regard to each individual member of the array. Again, this is a utility which would apply to virtually ever member of a general class of materials, such as any collection of proteins or DNA. Even if the expression of Appellant's individual polypeptide is affected by a test compound in an array for drug screening, the specification does not disclose any specific and substantial interpretation for the result, and none is known in the art. Given this consideration, the individually claimed polypeptide has no "well-established" use. The artisan is required to perform further experimentation on the claimed material itself in order to determine to what use any expression information regarding this polypeptide could be put.

Appellants assert the databases sold by Appellants' assignee, Incyte, include exactly the kinds of information made possible by the claimed invention, such as tissue and disease associations, Incyte sells its database containing the cloned sequence and millions of other sequences throughout the scientific community, including to pharmaceutical companies who use the information to develop new pharmaceuticals. Brief at 13.

However, this assertion fails to address the utility of the individually claimed polypeptide of the invention of the instant application. The claims are to isolated polypeptides, not to descriptive information included in a database. The commercial success of a database containing the sequence information of the claimed polypeptide does not confer a specific and substantial utility to the individual polypeptide as one of skill in the art would need to conduct further experimentation to determine the use of the individual member of the database.

Issue 3
Applicant argues that claim 1 recites not only that the variant polypeptides have at least 90% sequence identity to SEQ ID NO: 1, but also have "a naturally occurring amino acid sequence." Through the process of natural selection, nature will have determined the appropriate amino acid sequences. Thus, one skilled in the art need not make and test vast numbers of polypeptides that are based on the amino acid sequence of SEQ ID NO: 1. Instead, one skilled in the art need only screen a cDNA library or use appropriate PCR conditions to identify relevant polynucleotides/polypeptides that already exist in nature. Brief at 22.
The specification provides adequate guidance for making SEQ ID NO: 1 however the specification fails to provide guidance on use of this polypeptide sequence. As set forth in In re Fisher, 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:
that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

The unpredictability of the protein art is demonstrated in Voet (supra), which shows the large effect that even a single amino acid change can have on protein structure and function. This is a demonstration of the unpredictability of the protein art when trying to predict the function of a protein given only the primary amino acid sequence.
In Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016 (Fed. Cir. 1991), the court ruled that a claim to a large genus of possible genetic sequences encoding a protein with a particular function that needs to be determined subsequent to the construction of the genetic sequences may not find sufficient support under 35 USC 112, 1st paragraph, if only a few of the sequences that meet the functional limitations of the claim are disclosed and if undue experimentation would be required of one skilled in the art for determining other genetic sequences embraced by the claim. In the instant case there are a large number of polypeptide sequences which have 90% sequence identity to SEQ ID NO: 1 and are naturally occurring, however these sequences are various unrelated proteins, and no function is disclosed for the polypeptides encompassed by the claims. Therefore, while the specification provides the necessary guidance to make the polypeptide set forth in SEQ ID NO: 1 or polypeptide sequences which are 90% identical to SEQ ID NO: 1, it does not provide the necessary guidance for one of skill in the art to use the polypeptide sequence of SEQ ID NO: 1, or polypeptide sequences which are 90% identical to SEQ ID NO: 1. Further, since no function is associated with the HPURR protein encoded by SEQ ID NO: 1, one of ordinary skill in the art would not know how to use these defined sequences except in further characterization of the sequences themselves.

In view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time the invention was made, it would have required one of skill in the art undue experimentation to practice the invention as claimed.
Issue 4
Applicant argues that one of ordinary skill in the art would recognize polypeptide sequences which are variants having at least 90% amino acid sequence identity to SEQ ID NO: 1. Given any naturally occurring polypeptide sequence, it would be routine for one of skill in the art recognize whether it was a variant of SEQ ID NO:1, and that the subject matter of the present claims is defined in terms of the chemical structure of SEQ ID NO: 1. Brief at 25.
The instant claims are drawn to the polypeptide sequence of SEQ ID NO: 1, or polypeptide sequences which are 90% identical to SEQ ID NO: 1. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.
Considering all disclosed distinguishing identifying characteristics such as:
A: Partial structure - Only the structure of SEQ ID NO: 1 has been provided.

B: Physical and/or chemical properties - Only the physical or chemical properties of SEQ ID NO: 1 are provided.
C: Functional characteristics - The claimed the polypeptide sequence of SEQ ID NO: 1, or polypeptide sequences which are 90% identical to SEQ ID NO: 1 does not have a disclosed function, as set forth supra.
D: Known or disclosed correlation between structure and function - No structural/functional relationship is disclosed for the claimed polypeptide sequence of SEQ ID NO: 1, or polypeptide sequences which are 90% identical to SEQ ID NO: 1.
E: Method of making - Methods of making are disclosed.
F: Combinations of A-E - No combination of the other factors will adequately describe the claimed antagonist.
A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within a genus, one must describe a sufficient number of species to reflect the variation within the genus. What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. In an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus.
The specification does not describe sequences which have a biological function for any sequence 90% identical to SEQ ID NO: 1. Because the specification fails to describe more than a single species of each genus, and because one of skill in the art could not be expected to predict the biological activity of the sequence variants encompassed by the claims, the written description requirement has not been met. The specification provides a written description only for HPURR which is encoded by nucleic acids set forth in SEQ ID NO: 1.
Thus, in weighing all the factors in view of the level of skill and the knowledge in the art and in light of and consistent with the written description, one of skill in the art
would recognize from the disclosure that Applicant was not in possession of the claimed invention.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Joseph F. Murphy
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Conferees
Yvonne Eyler, SPE Art Unit 1646
Anthony Caputa, SPE Art Unit 1642

LEGAL DEPARTMENT
INCYTE PHARMACEUTICALS INC
3174 PORTER DRIVE
PALO ALTO, CA 94304

Application/Control Number: 09/096,070
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Art Unit: 1646

G.R. Ewoldt, Ph.D.
Patent Examiner
CM1, 9D06
703-308-9805